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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/900,751	Applicant(s) ALLEN ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *11/26/02* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 17-20 are pending examination.

Applicants' traversal, the cancellation of claims 1-16, the amendment to the abstract and the amendment to the specification, and the addition of claims 17-20 in paper no. 10 is acknowledged and considered.

The objections to the specification are moot in view of the amendments to the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 19 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility, a credible asserted utility or a well-established utility.

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS: repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" – Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, office personnel must determine if the assertion of utility is credible (i.e. whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based in inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific utility" – a utility that is *specific* to the subject matter claimed. This contrast with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what conditions can be diagnosed.

"Substantial utility" – a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying our further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic Research such as studying the properties of the claimed produce itself or the mechanisms in which the material is in involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. 101. This analysis should of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" – a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone, or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a non-specific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this were the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight, any carbon containing molecule would have a "well established utility" as a fuel since it can by burned; and any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

[See also the MPEP at 2107 –2107.02].

The claimed cell or tissue derived from a transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease is not supported by a specific asserted utility because the specification does not assert a utility for the cell or tissue.

Furthermore, the claimed cells and tissues are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, the claimed cell or tissue may be utilized to study serine protease gene function in individual development pathways. The need for such research clearly indicates that the cell or tissue and its function are not disclosed as to a currently available or substantial utility.

Note, the claimed invention is not supported by a specific and substantial utility because of the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for a cell or tissue derived from a transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease such that another non-asserted utility would be well established for the cell or tissue.

Applicants' traversal is not applicable to the rejection for claim 19 under 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility, a credible asserted utility or a well-established utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claim is rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention. The specification does not teach one skilled in the art how to use the claimed cell or tissue. The art of record is absent for using the claimed products. In addition, one skilled in the art would reasonably determine that the claimed products could be used for further experimentation on itself. However, further experimentation on itself is not considered a substantial utility, and the as-filed specification does not teach a 'real world' utility for the claimed cell or tissue. Thus in view of the In Re Wands Factors, the as-filed specification does not teach one skilled in the art how to use the claimed products.

Applicants' traversal is not applicable to the 112 enablement rejection for claim 19.

The rejection for claims 1-16 under 112 written description is moot in view of the cancellation of the claims.

Claims 17-18 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17-18 and 20, as best understood, are readable on a genus of a transgenic mouse comprising a disruption in an endogenous serine protease gene, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a

homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development, wherein the genus of a transgenic mouse is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of transgenic mice comprising a disruption in an endogenous serine protease gene. The starting material for making the claimed genus of transgenic mouse is a targeting construct comprising first and second polynucleotide sequences that are homologous to the serine protease gene. The as-filed specification states that, "serine protease gene" refers to a sequence comprising SEQ ID NO: 1 or comprising the sequence encoding the serine protease gene identified in GenBank Accession No. AF042822" (page 7). In addition, the disclosure defines "homologous" as a characteristic of a DNA sequence having at least 70% sequence identity as compared to a reference sequence (page 6). The specification provides sufficient description of a targeting vector comprising SEQ ID NO: 3 and 4 (see Figure 2B). However, the as-filed specification does not provide an adequate written description of a representative number of serine proteases and which disrupted serine protease would result in a developmental abnormality during embryonic development. This essential element (starting material) that is required for an adequate description of a representative number of species as embraced by the claimed genus is neither described sufficiently in the specification nor conventional in the prior art.

Furthermore, the specification provides sufficient description of a targeting vector that disrupts the serine protease set forth in SEQ ID NO: 1 and the transgenic mouse produce using the vector, however, the as-filed specification does not provide sufficient description of a representative number of targeting vectors beyond the vector that targets the protease gene corresponding to SEQ ID NO: 1. Therefore, in view of the lack of sufficient description of a genus of targeting vectors comprising nucleotide sequences for disrupting an endogenous serine protease, one skilled in the art could not envision that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is not sufficient to support the present claimed invention directed to a genus of a transgenic mouse comprising a disruption in an endogenous serine protease gene, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of transgenic mouse that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing,

or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus transgenic mouse that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicants' arguments are not applicable to the new rejection under 112 written description.

The rejection for claims 1-16 under 112 enablement is moot in view of the cancellation of the claims.

Claims 17-18 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing a transgenic mouse whose genome comprises a heterozygous disruption in the serine protease gene set forth in SEQ ID NO: 1 and breeding the mouse with a transgenic mouse with the same disruption to produce an embryo that dies between 12.5 and 14.5 days in the uterus, does not reasonably provide enablement for making a transgenic mouse whose genome comprises a disruption in any endogenous serine protease gene and using the mouse to produce a transgenic mouse having a homozygous disruption in an endogenous serine protease and exhibiting any developmental abnormality during embryonic

development. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of a transgenic mouse comprising a disruption in an endogenous serine protease gene, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development, particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. for producing a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development.

The claimed invention is directed to a method of produce a transgenic mouse comprising a disruption in an endogenous serine protease gene, wherein the transgenic mouse, upon breeding with another transgenic mouse whose genome comprises a heterozygous disruption in an endogenous serine protease gene, produces a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality

during embryonic development. The invention lies in the field of producing transgenic mice with a desired phenotype.

The state of the art at the time application was filed for producing transgenic mice with a desired phenotype using a knock out method was considered unpredictable. The unpredictability of predicting a phenotype in transgenic mouse is supported by Linder (Lab Animal, Vol. 30, pages 34-39, 2001) who states "It is critical to remember that the observed phenotype is not always the direct result of the genetic alteration". Linder further states, "The expression of a phenotype in mice carrying an induced mutation may depend on a number of factors not readily apparent to the initial researcher nor to those using the model in subsequent studies" (page 35).

The disclosure states that, "the serine proteases are a large family of proteolytic enzymes that include the digestive enzymes, trypsin, and chymotrypsin, components of the complement cascade and of the blood-clotting cascade" (page 1). The as-filed specification defines a serine protease gene as the polynucleotide sequence set forth in SEQ ID NO: 1. The specification states that a mouse gene encoding a new type of membrane bound serine protease (epithin, SEQ ID NO: 1) was isolated and sequenced by Kim et al. (IDS, 1999), see page 2. Kim teaches that, "The sequence was shown to be highly expressed in a thymic epithelial nurse cell line." Kim further teaches that they suspect that epithin will target either an extracellular matrix or another membrane bound protein on the same or neighboring cells.

The starting material required for producing the claimed transgenic mouse is a targeting construct comprising a) a first polynucleotide sequence homologous to a serine protease gene, b)

a second polynucleotide sequence homologous to the serine protease gene, and c) a selectable marker. The specification provides prior art pertaining to the preparation of transgenic mice (pages 11-13 and 15-18). For example, a transgene can be introduced into the germline of a transgenic mouse by microinjection for production of a transgenic mouse. The specification displays one method of generating a transgenic mouse: 1) A vector comprising the cDNA encoding SEQ ID NO: 1 and injected the vector into murine ES cells derived from 129/olaHsdby substrain (pages 51-52). Furthermore, the disclosure teaches that homozygous mutant embryos die between E12.5 and E14.5 (days) and no mutant mice were identified, whereas wild type and heterozygous mutant mice were present (pages 52-54).

In view of the In Re Wands Factors, the claimed invention is only enabled for a transgenic mouse whose genome comprises a heterozygous disruption in the serine protease gene set forth in SEQ ID NO: 1 and breeding the mouse with a transgenic mouse with the same disruption to produce an embryo that days within 2 weeks in the uterus. The claimed invention encompasses using transgenic mice having a heterozygous disruption in an endogenous serine protease to produce a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development. However, the specification teaches that no homozygous mice were identified only mutant embryos that die between 12.5 and 14.5 days in the uterus. Furthermore, in view of the large family of serine protease known in the art, the specification does not provide sufficient guidance of factual evidence for which endogenous serine protease can be disrupted resulting in embryo death between 12.5 and 14.5 days in the uterus. This

information is considered essential and is required for one skilled in the art to make and/or use the claimed invention. Since a mutant embryo is not a considered a transgenic mouse comprising a homozygous disruption in an endogenous serine protease gene, it would take one skilled in the art an undue amount of experimentation to reasonably correlate from producing a mutant embryo to producing a transgenic mouse with a homozygous disruption in an endogenous serine protease gene.

In addition, the specification does not provide sufficient guidance or factual evidence to enable one skilled in the art to make and use a genus of targeting vectors used to disrupt any endogenous serine protease gene functions in order to observe a developmental abnormality during embryonic development. As the specification fails to provide any relevant teachings or sufficient guidance with regard to the production of a representative number of targeting vectors for producing a genus of transgenic mice as claimed, one skilled in the art would not be able to rely on the state of the art for an attempt to produce any transgenic mouse whose genome comprises a homozygous disruption of an endogenous serine protease and exhibiting a dévelopmental abnormality (e.g. embryo death between 12.5 and 14.5 days in the uterus). This is because of the art of transgenic is not predictable art with respect to knock out methods for producing transgenic mice and the resulting phenotype. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic mouse comprising a disrupted endogenous serine protease gene; it is not predictable if the transgene would be expressed at a level and specificity

sufficient to cause a particular phenotype (e.g. embryo death between 12.5 and 14.5 days in the uterus). For example, the level and specificity of expression of the disrupted serine protease as well as the resulting phenotype of the transgenic mouse are directly dependent on the specific transgene construct.

In view of the reasons stated above, encompassing the absence of working examples for producing the claimed homozygous mouse and the concerns set forth by the art of record, it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the transgenic mouse in the working examples to a genus of transgenic mice whose genome comprises a disrupted endogenous serine protease gene with an embryonic developmental abnormality. Thus, the specification does not teach one skilled in the art how to practice the full scope of the claimed invention.

Furthermore, with respect to a transgenic mouse whose genome comprises a homozygous disruption of an endogenous serine protease and exhibiting a developmental abnormality during embryonic development, the as-filed specification only provides sufficient guidance or factual evidence for a developmental abnormality resulting in embryo death using a construct to disrupt the nucleotide sequence set forth in SEQ ID NO: 1. The term "developmental abnormality" embraces a large number of abnormalities (missing limb(s), abnormal size organ, psychological disorder, etc.) and the specification does not disclose any developmental abnormality other than embryo death between 12.5 and 14.5 days in the uterus using the method in the working example of the specification. In view of the reasons set forth above, it would take one skilled in the art an undue amount of experimentation to reasonably correlate from embryo death in the uterus to a

genus of developmental abnormalities. Thus, the full scope of the claimed embodiment is not enabled by the as-filed specification.

Furthermore, with respect to the method of producing a transgenic mouse, the claimed method is not enabled because step b) is missing the step of introducing a mouse embryonic stem cell into a blastocyst of a pseudopregnant mouse (see page 15 of the specification). The art of record teaches that stem cells do not develop into a mouse. However, the art of record teaches that in order to produce a transgenic mouse stem cells are injected into a blastocyst of pseudopregnant mouse. In addition, step c) of the claimed method embraces breeding the chimeric mouse to produce the transgenic mouse, but does not disclose using two transgenic mouse to produce a transgenic mouse having a homozygous disruption in an endogenous serine protease gene and exhibiting a developmental abnormality during embryonic development. The art of record teaches that breeding involves using two mice. Thus, the claimed method is not considered enabled for the reasons set forth above.

In addition, the specification does not provide sufficient guidance or factual evidence for how to produce a chimeric mouse. The specification describes chimeric mouse as "harbouring the homologously recombined DNA in their germ cells and can be used to breed animals in which all cells of the animal contain the homologously recombined DNA". For the reasons set forth above the specification is not enabled for producing the claimed chimeric mouse.

In conclusion, in view of the quantity of experimentation necessary to determine the parameters listed above for the starting material, a genus of transgenic mouse, the lack of direction or sufficient guidance provided by the as-filed specification for the production of any transgenic mouse, the claimed invention is only enabled for a transgenic mouse whose genome

comprises a heterozygous disruption in the serine protease gene set forth in SEQ ID NO: 1 and breeding the mouse with a transgenic mouse with the same disruption to produce an embryo that days within 2 weeks in the uterus and not the full scope of the claimed invention. Furthermore, the working examples for the demonstration or the reasonable correlation to the production of a genus of transgenic mouse using a knock-out method, in particular when the disruption of the serine protease must occur at a level resulting in a corresponding phenotype (e.g. embryonic developmental abnormality), it would require an undue amount of experimentation for one skilled in the art to make and/or use the full scope of the claimed invention.

Applicants' arguments are not found persuasive for the reasons of record set forth above.

The rejection for claims 5-9 and 11-16 under 112 second paragraph is moot in view of the cancellation of the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER